Decision Memo for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) has determined, based on the Food and Drug Administration (FDA) clearance of new embolic protection devices, to revise the national coverage determination (NCD) language regarding embolic protection devices as follows in section B3 and B4 of the NCD:

Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent and an FDA-approved or cleared embolic protection device for an FDA-approved indication when furnished in accordance with FDA-approved protocols governing post-approval studies. CMS determines that coverage of PTA of the carotid artery is reasonable and necessary in these circumstances.

Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent for the following:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis $\geq$70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or cleared embolic protection devices. *If deployment of the embolic protection device is not technically possible, and not performed, then the procedure is not covered by Medicare;*
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis $\geq$80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).

We have decided to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare NCD Manual 20.7B3 and B). We have decided to retain our existing coverage policy with a slight revision to the language regarding embolic protection devices.

Back to Top

Decision Memo

TO: Administrative File CAG-00085R7

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SUBJECT: Coverage Decision Memorandum for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7)

DATE: December 9, 2009

I. Decision

The Centers for Medicare and Medicaid Services (CMS) has determined, based on the Food and Drug Administration (FDA) clearance of new embolic protection devices, to revise the national coverage determination (NCD) language regarding embolic protection devices as follows in section B3 and B4 of the NCD:

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We have decided to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare NCD Manual 20.7B3 and B). We have decided to retain our existing coverage policy with a slight revision to the language regarding embolic protection devices.

II. Background

CMS internally generated this reconsideration request for PTA of the carotid artery concurrent with stenting. In the last reconsideration on this topic on October 14, 2008 (CAG-00085R6) CMS stated that "[w]e are aware of other data that has yet to be published and strongly urge that publication at the soonest possible time. We will work with any requestor as soon as that data is published to determine the need for an expedited review and reconsideration." New data have recently been published that examine outcomes in patients for whom coverage is currently limited to participation in clinical trials and post approval studies. In this reconsideration, CMS examines whether coverage should be expanded to beneficiaries who are at high risk for adverse events related to CEA due to anatomic risk factors with asymptomatic carotid artery stenosis of $\geq$ 80% when CAS procedures are performed outside of clinical trials, FDA approved IDE trials or FDA approved post approval studies. Throughout this document we reference patients who are at high risk due to CEA. When we make this statement we are discussing patients who are at high risk for adverse outcomes if they undergo CEA. These patients may be at high risk for adverse outcomes due to physiologic conditions or anatomic conditions. A list of conditions that cause patients to be at high risk for adverse outcomes if they undergo CEA is provided in the full text of the NCD (Appendix B).

Under the current policy patients at high risk for CEA who have symptomatic carotid artery stenosis ≥ 70% are covered for procedures performed using FDA approved CAS systems with embolic protection devices in facilities approved by CMS to perform CAS procedures. In addition, patients at high risk for CEA with symptomatic carotid artery stenosis between 50% and 70% and patients at high risk for CEA with asymptomatic carotid artery stenosis ≥ 80% are covered in accordance with the Category B IDE clinical trials regulation (42, CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post approval studies (Medicare NCD Manual 20.7, B3).

III. History of Medicare Coverage

Over the past eight years, Medicare has expanded coverage for PTA and stenting of the carotid artery. Medicare first covered PTA of the carotid artery concurrent with stent placement in accordance with the FDA approved protocols governing Category B IDE clinical trials and later in FDA required post approval studies (Medicare NCD Manual 20.7B2, B3).

Effective March 17, 2005, Medicare expanded coverage for PTA and stenting of the carotid artery when performed on patients at high risk for CEA who also have symptomatic carotid artery stenosis ≥ 70% only when performed in a CMS approved facility for CAS with FDA-approved carotid artery stenting systems and embolic protection devices. Symptoms of carotid artery stenosis include carotid transient ischemic attack (TIA) (distal focal neurological dysfunction persisting less than 24 hours), non-disabling stroke (Modified Rankin Scale score < 3 with symptoms for 24 hours or more), and transient monocular blindness (amaurosis fugax) (Medicare NCD Manual 20.7B4).

Effective April 30, 2007, Medicare maintained the existing coverage policy and included detailed facility recertification instructions in the NCD.

Effective October 14, 2008, Medicare maintained the existing coverage policy, making no deletions, revisions or additions.

Medicare’s NCD for PTA concurrent with carotid stenting can be found in NCD Manual 20.7. Medicare’s NCD for PTA concurrent with carotid stenting in FDA approved post approval studies can also be found in NCD Manual 20.7B3.

Benefit Category Determination

For an item or service to be covered by the Medicare program, it must fall within one of the statutorily defined benefit categories outlined in the Social Security Act. PTA of the carotid artery concurrent with stenting, at a minimum, falls under the benefit categories set forth in section §1861(b) (inpatient hospital services), a part A benefit under §1812(a)(1) and §1861(s)(1) (physician services), a part B benefit. This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

IV. Timeline of Recent Activities

March 18, 2009	CMS internally generated a reconsideration request to examine newly published evidence.
April 17, 2009	Initial 30-day public comment period closed.
September 10, 2009	Proposed decision memorandum posted; 30-day comment period begins.

V. FDA Status

There are currently seven carotid stent systems with Premarket Approval (PMA) approval by the FDA plus five distal filter embolic protection devices (EPDs) and one distal balloon occlusion EPD with FDA 510(k) clearance. Recent FDA 510(k) cleared EPDs include one proximally placed flow reversal EPD and one distally placed filter with focal suction.[1,2]

VI.General Methodological Principles

When making national coverage decisions, under §1862(a)(1)(A), CMS generally evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

In this coverage analysis, we considered carotid artery stenting studies and evidence that were published since the last reconsideration in 2008. It incorporates all evidence from prior decision memoranda regarding this issue. A summary of the body of evidence reviewed to date in developing this decision memorandum is available via the final decision memoranda released following the completion of each of the prior national coverage analyses (NCAs) for reconsiderations of the CAS NCD. For carotid artery stenting, we believe that studies should evaluate health outcomes especially in patients who do not have symptoms from carotid artery disease. Health outcomes for carotid artery stenting include death, stroke, myocardial infarction and other adverse events.

As noted in the two prior reconsiderations of this topic, we have considered the professional society guidance that the accepted standards for carotid revascularization should apply to CAS if it is to be considered an alternative to CEA. Professional guidelines developed and published by the American Heart Association (AHA) (Sacco, et al., 2006; Goldstein et al., 2006) identify these benchmarks and suggest that CEA is indicated in patients with asymptomatic and symptomatic carotid artery stenosis when surgeons can achieve perioperative morbidity and mortality rates that are < 3% and < 6% respectively. Similar periprocedural rates would be expected to demonstrate that CAS improves health outcomes.

Literature Search

Because this is a reconsideration, CMS focused on new clinical research studies, technology assessments, guidelines and reviews published since the October 14, 2008 decision memorandum, but also considered literature addressing the patient populations under consideration which was published prior to the 2008 NCD. CMS searched PubMed from January 2008 to October 2009. General keywords included carotid artery stenting, carotid artery angioplasty, risk factors (high risk for surgery and anatomic risk factors). Abstracts without a complete publication were excluded. Using these general parameters, 10 original studies, 2 systematic reviews and 3 sets of evidence based guidelines were found.

B. Discussion of evidence reviewed

1. Evidence Questions

Our determination of whether to expand coverage of carotid artery stenting for high risk asymptomatic patients under Medicare involves consideration of health outcomes. For this NCD, the questions of interest are:

a. Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients at high risk for adverse events related to CEA with carotid artery stenosis $\geq$ 80% improves health outcomes compared to carotid endarterectomy or optimal medical therapy outside the clinical trial or post market study setting?

b. Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors for CEA associated adverse events with carotid artery stenosis $\geq$ 80% and symptomatic patients with carotid artery stenosis 50-70% improves health outcomes?

2. External Technology Assessments

Abbott AL. Medical (Nonsurgical) Intervention Alone Is Now Best for Prevention of Stroke Associated With Asymptomatic Severe Carotid Stenosis Results of a Systematic Review and Analysis. Stroke 2009;40:e573-e583.

Abbott reported the results of a systematic review with 3 specific objectives:

1. "To investigate temporal changes in reported stroke (+/-TIA) rate and baseline characteristics among patients with asymptomatic severe carotid stenosis receiving medical intervention alone."

2. "To compare the above stroke (+/-TIA) rates with those of patients who received CEA in major randomized surgical trials."

3. "To compare stroke prevention cost-effectiveness of current medical intervention alone with medical intervention and CEA as employed in major randomized surgical trials."

The author included 11 studies (3724 patients with mean age of 66 years). Kaplan–Meier risk estimates were calculated. The author reported: "Significant advances in vascular disease medical intervention since large randomized trials for asymptomatic severe carotid stenosis were conducted (1983–2003) have prompted doubt over current expectations of a surgical benefit. In this systematic review and analysis of published data it was found that rates of ipsilateral and any-territory stroke (+/-TIA), with medical intervention alone, have fallen significantly since the mid-1980s, with recent estimates overlapping those of operated patients in randomized trials. However, current medical intervention alone was estimated at least 3 to 8 times more cost-effective. In conclusion, current vascular disease medical intervention alone is now best for stroke prevention associated with asymptomatic severe carotid stenosis given this new evidence, other cardiovascular benefits, and because high-risk patients who benefit from additional carotid surgery or angioplasty/stenting cannot be identified." While this review focused on CEA, it is relevant to CAS since it is also considered carotid intervention.

Ederle J, Featherstone RL, Brown MB. Randomized controlled trials comparing endarterectomy and endovascular treatment for carotid artery stenosis: a Cochrane systematic review. Stroke 2009;40:1373-1380.

Ederle and colleagues reported the results of a Cochrane systematic review "to assess the benefits and risks of endovascular treatment compared to surgery." This review provided an update of the Cochrane review done by the same authors in 2007 which reported that the data were "limited and conflicting" and concluded that: "The data support the continuing inclusion of patients within randomized clinical trials between endovascular and surgical treatment for carotid artery stenosis. Randomisation should continue in the ongoing trials and centres not participating in the large multicentre trials should be encouraged to randomise suitable patients locally. This could contribute to any future meta-analysis."

For the current review, randomized trials on stenting compared to endarterectomy were selected. Only randomized trials were included so the published registry studies were not. Ten trials (n=3178 patients) were included in the analysis. The primary outcome was stroke or death within 30 days. Intention to treat analysis was used. The Peto fixed effect model was used to calculate odds ratios. The authors found: "Using a fixed-effect model, the odds ratio (OR) for the combined outcome of death or any stroke was significantly in favor of carotid endarterectomy (OR endovascular:surgery 1.40, 95% CI 1.04 to 1.88, P = 0.03)." Identical to the 2007 review, they concluded: "The data are difficult to interpret because the trials are heterogeneous. Five trials were stopped early, perhaps leading to an overestimate of the risks of endovascular treatment. The results do not support a change in clinical practice away from recommending carotid endarterectomy as the treatment of choice for suitable carotid artery stenosis but support continued recruitment in the large ongoing trials."

3. Internal Technology Assessment

Chiam PTL, Roubin GS, Panagopoulos G, Iyer SS, Green RM, Brennan C, Vitek JJ. One-year clinical outcomes, midterm survival, and predictors of mortality after carotid stenting in elderly patients. Circulation 2009;119:2343 -2348.

Chiam and colleagues reported the results of a case series (n=142) of elderly patients who underwent CAS from 2003 to 2007 "to determine survival and predictors of mortality of selected elderly patients after stenting." Inclusion criteria were age ≥ 80 years and symptomatic ≥ 50% diameter stenosis or asymptomatic stenosis ≥ 70%. Patients were non high risk patients. The outcomes included combined death and stroke at 30 days and death at 12 months. Mean age was 83 years. Men comprised 61%. Symptomatic patients comprised 28%.

The authors reported: "Among the 153 procedures, 5 events (1 death, 2 major strokes, 2 minor strokes) occurred, resulting in an overall 30-day stroke or death rate of 3.3% (5.1% in the symptomatic group, 2.6% in asymptomatic patients)." At 12 months, 15 (12%) deaths occurred out of 129 patients with at least 1 year of follow-up. The authors concluded: "This study demonstrates that in selected elderly patients, a high proportion (85%) survived 2 years and >75% survived 3 years after stenting. Carotid stenting may be considered a revascularization option in such patients. Better selection of patients using the predictors of mortality may help to reduce unwarranted procedures and to optimize survival likelihood." Limitations of case series such as selection issues and lack of controls are applicable. Results by symptomatology and anatomic risk factors were not reported. At 12 months, there were 15 deaths and 1 nonfatal stroke for a combined 12.4% (16/129) rate. Although these patients were considered non high risk, the authors noted: "Elderly patients undergoing CS, however, may not represent the "average" elderly patient. No data on survival after CS in elderly patients are available."

de Donato G, Setacci C, Deloose K, Peeters P, Cremonesi A, Bosiers M. Long-term results of carotid artery stenting. J Vasc Surg 2008;48:1431-1441.

de Donato and colleagues reported the results of an analysis of a registry of 4 European carotid high volume centers (n=3179) "to review long-term results after carotid stent implantation in a large cohort of patients." Patients underwent CAS from 1998 to 2006. Inclusion criteria included "symptomatic lesions ≥ 50%, asymptomatic lesions ≥ 80%, calculated according to the North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria." Outcomes included death, stroke or other neurological complications. Mean age was about 72 years. Men comprised 67%. Symptomatic patients comprised 41%.

The authors reported: "At 5 years freedom from mortality, stroke-related death, ipsilateral fatal/major stroke, and any stroke rate were 82%, 93.5%, 93.3%, and 91.9%, respectively." Rates of all cause mortality and any stroke increased year to year and were similar for symptomatic and asymptomatic patients. The authors concluded: "Our long-term results in a large cohort of patients validated CAS as a durable procedure for stroke prevention. The annual rate of neurological complications after CAS was comparable to that of conventional surgery as demonstrated by large RCTs involving both symptomatic patients (North American Symptomatic Carotid Endarterectomy Trial [NASCET] and European Carotid Surgery Trial [ECST]) and asymptomatic patients (Asymptomatic Carotid Atherosclerosis Study [ACAS] and Asymptomatic Carotid Surgery Trial [ACST])." Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable. The stroke and death proportions for asymptomatic patients were 3.5%, 8.2%, 15.4%, 20.1% and 26.1% from years 1 to 5 respectively. The authors reported a 1.9% annual rate of stroke. Results by anatomic risk factors were not reported. Surgical risk was not an inclusion criterion.

Ederle J, Featherstone RL, Brown MM, CAVATAS collaborators. Long-term outcome of endovascular treatment versus medical care for carotid artery stenosis in patients not suitable for surgery and randomized in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS). Cerebrovascular Diseases 2009;23:1-7.

Ederle and colleagues reported the results of a randomized controlled trial of patients (n=40) considered unsuitable for carotid endarterectomy in CAVATAS to compare endovascular treatment of carotid stenosis to medical treatment. Patients included in CAVATAS had the "presence of clinically important carotid stenosis" as determined by the individual site investigators. Patients considered unsuitable for CAVATAS had "recent myocardial infarction, poorly controlled, hypertension or diabetes mellitus, renal disease, respiratory failure, inaccessible carotid stenosis, or severe cervical spondylosis" and were randomized (1:1) to carotid intervention (n=20) or medical therapy (n=20) for this subset trial (CAVATAS-MED). Of the 40 patients, 17 patients had surgical contraindications, 14 had medical contraindications, 7 refused surgery and 2 had unrecorded reasons for why they were considered unsuitable for surgery. Primary outcome was death or stroke in the follow-up period. Patients were enrolled from 1992 to 1997. Intention to treat analysis was used. Mean age was about 69 years. Men comprised 78%. Symptomatic patients comprised 63%. Median follow-up was 4.5 years.

The authors found 1 death or stroke within 30 days in the endovascular treatment group and 0 death or stroke within 30 days in the medical group. At any time during the follow-up period, there were 9 death or stroke events in both groups. The authors concluded: "We failed to show superiority of endovascular treatment above medical care alone for carotid stenosis in a very small group of patients not suitable for surgical treatment. However, the trial randomized only 40 patients, and was therefore severely underpowered to detect clinically relevant treatment differences. Ongoing trials of carotid stenting will need to demonstrate improved safety and efficacy before endovascular treatment should enter routine practice." In this report, the inclusion criteria were not well defined. Since enrollment started before stents were available, endovascular treatment was variable. The actual number of patients who underwent CAS was not reported. Medical therapy also was not uniformly defined. Results for symptomatic and asymptomatic patients were not reported separately.

Gray WA, Chaturvedi S, Verta P, on behalf of the Investigators and the Executive Committees. Thirty-day outcomes for carotid artery stenting in 6320 patients from 2 prospective, multicenter, high-surgical-risk registries. Circ Cardiovasc Intervent 2009;2:159-166.

Gray and colleagues reported the results of a combined analysis of "2145 patients from the Emboshield and Xact Post Approval Carotid Stent Trial (EX) and 4175 patients from the Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events (C2)." The objective was to evaluate how outcomes from CAS compared to perioperative morbidity (stroke) and mortality recommendations from the American Heart Association and the American Stroke Association on prevention of stroke in symptomatic and asymptomatic patients (see guidelines in section 5 below). Patients were high-surgical risk individuals who underwent CAS from 2004 to 2006 and had symptomatic (≥ 50% stenosis) or asymptomatic (≥ 80% stenosis) lesions. Of the 6370 patients enrolled in the EX [3] and C2 [4] postmarket surveillance studies mandated by the FDA, 6320 patients were included in the analytical dataset. The EX study involved 253 investigators at 128 sites while the C2 study involved 519 investigators at 186 sites. The primary end point of both studies was a composite of death, stroke or myocardial infarction within 30 days of CAS. Mean age was about 73 years. Men comprised about 62% of the subjects. Patient with symptoms of carotid artery stenosis comprised about 12%.

The authors reported: "The 30-day primary composite end point (hierarchical) of death, stroke, and MI for EX was 4.1% (95% CI, 3.3% to 5.1%), for C2 was 3.7% (95% CI, 3.1% to 4.3%), and for the combined studies was 3.8% (95% CI, 3.4% to 4.3%). The 30-day combined end point of death and stroke rate for EX was 4.1% (95% CI, 3.3% to 5.0%), 3.4% (95% CI, 2.9% to 4.0%) for C2, and 3.6% (95% CI, 3.2% to 4.1%) for the combined population. For the combined symptomatic population the rate of 30-day death and stroke was 6.4% (95% CI, 4.8% to 8.4%), and for the combined asymptomatic population it was 3.2% (95% CI, 2.8% to 3.7%)."

A subgroup analysis of patients with anatomic high surgical risk factors ("history of CEA, radiation, therapy to the neck or radical neck surgery, surgically inaccessible lesion at or above the C2 vertebra or below the clavicle, lesions obstructed by tumors in the neck, spinal immobility/inability to flex neck beyond neutral or kyphotic deformity, the presence of a tracheostomy stoma, and contralateral laryngeal nerve palsy") was also performed. They reported: "The 30-day rate of death and stroke for the 60 symptomatic patients with anatomic factors was 1.7% (95% CI, 0.0% to 8.9%); the single stroke was adjudicated as major. The 30-day rate of death and stroke for the 371 asymptomatic patients with anatomic high-risk features was 2.7% (95% CI, 1.3% to 4.9%), of which 78% were minor."

The authors concluded: "Outcomes for carotid artery stenting in nonoctogenarian high-surgical-risk patients have improved since the pivotal Food and Drug Administration approval trials, and have achieved American Heart Association standards in both symptomatic and asymptomatic lesions." They also reported: "This study also carries the limitations of any registry analysis, including limited follow-up duration and the potential for bias in end point detection. Given that any prophylactic procedure requires the patient to survive long enough to reap the benefit of reduced end point events to justify procedural or surgical risk (as per the AHA guidelines document stipulation of an expected 5-year survival), no definitive statements regarding the ultimate benefit of CAS can be made absent long-term follow-up in this population. Last, the separation of patients between high-risk anatomic and physiological features is complex because of the need to rank order the risk factors for categorization (ie, a patient may have both an anatomic and physiological risk), resulting in almost twice the number of octogenarians in the physiological group, and potentially contributing to an increase in outcome events in this cohort."

Groeneveld PW, Yang L, Greenhut A, Yang F. Comparative effectiveness of carotid arterial stenting versus endarterectomy. J Vasc Surg 2009;50:1040-8.

Groeneveld and colleagues reported the results of a retrospective cohort study to "compare the effectiveness of CAS to CEA in a nonexperimental, nationwide population of Medicare beneficiaries receiving carotid revascularization after the March 2005 Medicare coverage expansion for CAS." Medicare fee for service claims from 2002 to 2006 were examined. ICD-9 codes (00.55, 39.90; 0.061, 0.063) were used to create CAS comparison groups and the CEA group (38.12). Patients who had claims for CAS from October, 2002 to September, 2004 (n=4590; 3% of carotid revascularization patients for the specified time frame) were entered into the "pre-coverage era" group, while patients had claims for CAS from August, 2005 to March, 2006 (n=5354; 11% of carotid revascularization patients for the specified time frame) were entered into the "coverage era" group. Outcomes included mortality, acute myocardial infarction and stroke. Comparisons were performed between areas with high CAS adoption (23% of carotid procedures were CAS) and low adoption (9% were CAS). Propensity scores were used to match patients across eras. Mean age was 76 years. Men comprised 60% of the cohorts. Less than 4 % of patients had a prior diagnosis of stroke or TIA.

The authors found no significant difference in 270 day mortality (4.8% coverage era versus 4.6% pre-coverage; P=0.17) but a significant difference in combined outcome of stroke, death, acute myocardial infarction (7.7% coverage era versus 7.3% pre-coverage; P=0.17). They reported: "In localities with higher adoption of carotid stents, there was higher 90-day mortality (adjusted odds ratio [OR] 1.15; P = .16), 90-day combined outcomes (OR = 1.17; P = .03), 270-day mortality (OR = 1.13; P = .07), and 270-day combined outcomes (OR = 1.10; P = .09) in the coverage era." They concluded: "The adoption of carotid stents for treatment of carotid stenosis was associated with increased rates of adverse clinical outcomes after carotid revascularization." As with many studies using administrative claims data, specific clinical information such as symptoms from carotid stenosis or surgical risk factors may not be coded and unavailable in claims data, thus making the matching of cohorts more difficult. Unadjusted differences in the patient cohorts in the high and low adoption areas may potentially influence results. The stroke or death rate was not reported separately. Medical therapy is also difficult to determine in earlier claims data.

Kawabata Y, Sakai N, Nagata I, Horikawa F, Miyake H, Ueno Y, Kikuchi H. Clinical predictors of transient ischemic attack, stroke, or death within 30 days of carotid artery stent placement with distal balloon protection. J Vasc Interv Radiol 2009;20:9–16.

Kawabata and colleagues reported the results of a case series of 58 patients who underwent carotid artery stenting from 1999 to 2008 "to determine potential clinical risk factors for the development of postprocedural neurologic deficits after carotid artery stent placement." Inclusion criteria included $\geq$ 50% carotid stenosis if they had recurrent stroke or $\geq$ 60% carotid asymptomatic stenosis with bilateral carotid lesions or multiple-vessel disease. Primary outcome was combined 30 day major adverse events. Of the 58 patients, 41 were high risk while 17 were low risk. Mean age was 70 years. Men comprised 84%. Symptomatic patients comprised 52%.

The authors reported: "Six patients (9.0%) experienced a TIA and one patient (1.5%) had a major stroke (1.5%) within 30 days of the procedure." The 30 day stroke and death rate was 1.5%. They concluded: "Our data suggest that carotid artery stent placement with distal balloon protection can be performed with similar periprocedural complication rates as CEA. CEA should be the first-line treatment in the management of patients older than 75 years of age." Limitations inherent to case studies are applicable. Sample size was small. Low risk patients were included which may lead to reduced 30 day events. Anatomic high risk factors were not evaluated.

Massop D, Dave R, Metzger C, Bachinsky W, Solis M, Shah M, et al. Stenting and angioplasty with protection in patients at high-risk for endarterectomy: SAPPHIRE Worldwide Registry first 2,001 patients. Catheterization and Cardiovascular Interventions 2009;73:129–136.

Massop and colleagues reported the results of an interim analysis of the SAPPHIRE[5] (Stenting and Angioplasty with Protection of Patients with High Risk for Endarterectomy) Worldwide registry (n=2001) "to evaluate 30-day outcomes after CAS utilizing the CASES training program within a broader number of centers and an increased number of physicians performing the procedure." The SAPPHIRE Worldwide registry (SAPPHIRE WW[6]) is a post market study being conducted at 350 clinical sites (216 contributed data) in the U.S. and Canada. The primary end point was a composite of death, stroke or myocardial infarction within 30 days of CAS. High surgical risk patients were required to have "either $\geq$ 50% carotid stenosis (as determined by ultrasound or angiogram) if symptomatic (TIA or stroke within 180 days of the procedure) or $\geq$ 80% carotid stenosis (as determined by ultrasound or angiogram) if asymptomatic." Of the 2001 patients enrolled from 2006 to 2008, 1620 had complete 30 day follow up data and were included in the analysis. Mean age was about 72 years. Men comprised 62%. Patients with symptoms of carotid stenosis comprised 28%.

The authors reported: "The cumulative incidence of MAE at 30 days was 4.4% (95% CI 3.5%, 5.3%), a rate comparable to the MAE rates in previous studies." The rate of death and stroke was 4.0% at 30 days. They also reported: "Asymptomatic patients with anatomic risk factors had a 30-day stroke and death rate of 1.8% while symptomatic patients with anatomic risk factors had a 30-day rate of 4.5% (P=0.0589)." They concluded: "While the number of physicians performing CAS continues to increase, MAE rates seen in this registry (4.4%) are well within an acceptable range, as was first seen in the SAPPHIRE randomized trial (4.8%). A significant decrease in MAE was seen in patients with anatomic risk compared with physiologic risk factors. The SAPPHIRE Worldwide Registry supports the use of CAS as an alternative to CEA in patients who are at high-risk for surgery due to anatomic risk factors." Overall results were not reported separately for asymptomatic and symptomatic patients. The most common anatomic risk factors were previous CEA restenosis and contralateral carotid occlusion. Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable.

Sidawy AN, Zwolak RM, White RA, Siami FS, Schermerhorn ML, Sicard GA, et al. Risk-adjusted 30-day outcomes of carotid stenting and endarterectomy: Results from the SVS Vascular Registry. J Vasc Surg 2009;49:71-79.

Sidawy and colleagues reported the results of an analysis of the Society for Vascular Surgery (SVS) Vascular Registry (VR), the "the first operational societal registry of carotid procedures" with 1450 CAS patients, "to report the feasibility of the VR and to provide the baseline demographics and risk-adjusted 30-day outcomes of CAS and CEA." Patients underwent carotid intervention from 2005 to 2007. Specific inclusion and exclusion criteria were not reported. The VR contained data from 287 providers at 56 centers at time of the publication. The primary outcome was combined death, stroke and myocardial infarction at 30 days. Of the CAS patients, mean age was about 71 years. Men comprised 60%. Symptomatic patients comprised 44%.

The authors reported: "For CAS, death/stroke/MI at 30 days was 7.13% for symptomatic patients and 4.60% for asymptomatic patients (P=.04)." The combined rate was 5.7% (83/1450) and the death and stroke rate at 30 days was 5.6% (81/1450). The authors concluded: "Following best possible risk adjustment of these unmatched groups, symptomatic and asymptomatic CAS patients had significantly higher 30-day postprocedure incidence of death/stroke/MI when compared with CEA patients. The initial 1.5 years of data collection provide proof of concept that a specialty society based VR can succeed in meeting regulatory and scientific goals. With continued enrollment and follow-up, analysis of SVS-VR will supplement randomized trials by providing real-world comparisons of CAS and CEA with sufficient numbers to serve as an outcome assessment tool of important patient subsets and across the spectrum of peripheral vascular procedures." Results by anatomic risk factors were not reported. Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable.

Simonetti G, Gandini R, Versaci F, Pampana E, Fabiano S, Stefanini M, et al. Carotid artery stenting: findings based on 8 years' experience. Radiol med 2009;114:95–110.

Simonetti and colleagues reported the results of a registry of 1003 patients who underwent CAS from 1999 to 2007 to evaluate 30 day death and stroke. Inclusion criteria were symptomatic stenosis > 50% and asymptomatic lesions with stenosis > 70%, in agreement with the NASCET criteria. Primary outcome was combined 30 day death and stroke. Mean age was 70 years. Men comprised 58%. High risk patients "refused by surgeons" comprised 24%. Symptomatic patients comprised 52%.

The authors reported: "The 30-day transient ischaemic attack (TIA)/stroke/death rate was 2.16%: death (0.18%) major stroke (0.45%) and minor stroke/TIA (1.53%). During a follow-up up to 8 years, restenoses occurred in 39 cases (3.57%), of which 28 were post-CAS (2.57%) and 11 post-CAS performed for restenosis after carotid endarterectomy (1%)." Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable. Low risk patients were included which may lead to reduced adverse event rates. Definitions of low and high risk were not specified. Anatomic high risk factors were not evaluated.

Steppacher R, Csikesz N, Eslami M, Arous E, Messina L, Schanzer A. An analysis of carotid artery stenting procedures performed in New York and Florida (2005-2006): Procedure indication, stroke rate, and mortality rate are equivalent for vascular surgeons and nonvascular surgeons. J Vasc Surg 2009;49:1379-86.

Steppacher and colleagues reported the results of an analysis of inpatient data from New York and Florida (n=4001) to compare "the indications, in-patient mortality rate, and in-patient stroke rate for patients undergoing CAS, according to operator specialty." Patients were identified by querying inpatient databases from the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Health Care Research and Quality (AHRQ) for International Classification of Disease (ICD)-9-CM codes 00.63 (carotid artery stenting) and 00.61 (carotid artery angioplasty) from 2005-2006. Outcomes included inpatient death and stroke. Symptomatic patients were identified using codes for "transient ischemic attack, amaurosis fugax, or stroke at the time of admission." Mean age was about 71 years. Men comprised 62%. Symptomatic patients comprised 9%.

The authors reported overall inhospital mortality and stoke of 2.0%. For symptomatic patients (n=348), the inhospital mortality and stroke was 7.8%. The authors concluded: "Despite a paucity of level 1 evidence for CAS in asymptomatic patients and current Centers for Medicare and Medicaid Services (CMS) policy limiting reimbursement for CAS to only high-risk symptomatic patients, VS (vascular surgeons) and non-VS are treating primarily asymptomatic patients. Perioperative rates of stroke and death are equivalent between VS, IC (interventional cardiologists), and IR (interventional radiologists). Regional variation of operator type is substantial, and despite similar outcomes, < 50% of CAS is performed by VS." Results for asymptomatic patients were not reported. Limitations include those inherent to hospital discharge databases, coding accuracy, difficulties classifying symptom class and lack of data on degree of stenosis. Data were only available for the hospital stays which may not reflect 30 day outcomes in many instances.

Usman AA, Tang GL, Eskandari MK. Metaanalysis of procedural stroke and death among octogenarians: carotid stenting versus carotid endarterectomy. J Am Coll Surg 2009;208:1124-1131.

Usman and colleagues conducted "a metaanalysis on 41 sets of data from peer-reviewed published articles on CAS versus CEA in octogenarians from 1997 to 2007" and "compared the primary outcomes measures of periprocedural (30-day) myocardial infarction (MI), stroke, and death after CAS or CEA in patients aged 80 years or greater for all studies." Studies were included if 10 or more procedures were performed, 30 day outcomes were reported and 30 day complication rates were available. Eight stenting studies (826 patients) and 33 endarterectomy studies (7017 patients) were evaluated. The authors reported: "In conclusion, octogenarians undergoing CAS had a 3.46-times higher absolute risk of stroke than those undergoing CEA, with no significant difference in mortality and a trend toward a lower rate of MI. Further outcomes research and risk stratification analyses are needed to help guide clinical decision-making. But given that the purpose of carotid intervention is stroke prevention, CAS in octogenarians using current technology should be avoided in favor of CEA or possibly medical management unless a stroke rate of less than 3% can be achieved."

Vogel TR, Dombrovskiy VY, Haser PB, Scheirer JC, Graham AM. Outcomes of carotid artery stenting and endarterectomy in the United States. J Vasc Surg 2009;49:325-330.

Vogel and colleagues reported the results of an analysis of carotid artery stenting outcomes based on inpatient data from the 2005 Nationwide Inpatient Sample (NIS) "to evaluate national outcomes of CAS and CEA and to compare utilization and outcomes of these procedures in different age groups." The NIS is an "all-payer hospital database developed as part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Health Care Research and Quality (AHRQ)." Patients were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code 00.63 for CAS. The analytic database included 6569 patients aged 60 years and older who underwent CAS. Mean age was about 73 years. Men comprised 62%. Symptomatic patients comprised 2.9% (189/6569) and were identified using codes for transient cerebral ischemia, transient paralysis of limb, transient arterial occlusion, transient visual loss, amaurosis fugax and other generalized ischemic cerebrovascular disease.

The authors reported: "The overall incidence of stroke was 4.16% after CAS and 2.66% after CEA ($P < .0001$). CAS was more often utilized in octogenarians than in younger patients (8.55% in 80+ vs 7.92% in 60-69 years; $P < .0002$). Increased age was not associated with greater stroke rates after CAS or CEA ($P=.19$ and .06, respectively). Octogenarians, compared to younger patients, had greater cardiac, pulmonary, and renal complications after CEA (3.0% vs 1.9%, 1.9% vs 1.0%, and 1.4% vs 0.54%, respectively; $P < .0001$)." They found a death and stroke rate of 298/6569 (4.5%) during the inpatient stay for CAS and concluded: "Octogenarians did not have a higher risk of stroke after CAS when compared to younger patients. Stroke was the strongest predictor of hospital mortality. The increased utilization of CAS in the aged, which had significantly higher stroke rates in all age groups studied, may account for the greater hospital mortality seen after CAS in the elderly. Further studies focused on the aged are needed to define the best management strategies in the elderly." Results were not reported by symptomatology although there were very few patients identified as symptomatic patients. Limitations include those inherent to hospital discharge databases, coding accuracy, difficulties classifying symptom class and lack of data on degree of stenosis. Data were only available for the hospital stays which may not reflect 30 day outcomes in many instances.

Zarins CK, White RA, Diethrich EB, Shackelton RJ, Siami FS for the CaRESS Steering Committee and CaRESS Investigators. Carotid revascularization using endarterectomy or stenting systems (CaRESS): 4-year outcomes. J Endovasc Ther 2009;16:397–409.

Zarins and colleagues reported 4 year outcomes of the Carotid Revascularization using Endarterectomy or Stenting Systems (CaRESS), a "prospective, nonrandomized comparative cohort study of a broad-risk population of symptomatic and asymptomatic patients with carotid stenosis" (initial article in 2003; http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=157). Of the total 397 patients, 184 were considered high risk for surgery (107 CEA; 77 CAS patients). Of these, 12 patients had symptomatic stenosis of 50-74% and 133 had asymptomatic stenosis $\geq$ 75%. For this subset of 145 patients who met CMS' entry criteria, the authors reported: "There was no difference in death/stroke rates between CEA (3.6%) and CAS (1.7%) at 30 days or at 4 years (CEA 31.5% and CAS 33.5%)." Rates for symptomatic and asymptomatic patients were not presented for this small subgroup. For all 397 patients, 4 year death/stroke rates were 12.4% (5/44) and 25.8% (22/99), respectively. For patients > 80 years of age, 4 year death/stroke rates were 35.4% (13/52) for CEA and 54.1% (13/25) for CAS. The sample sizes for these subgroups were small.

4. MEDCAC

No Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) was convened for this issue.

5.Evidence-based guidelines

Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JVI, Sacco RL. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: Cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Stroke 2006;37:1583-1633.

This guideline provided "an overview of the evidence on various established and potential stroke risk factors and provides recommendations for the reduction of stroke risk." Specifically for asymptomatic carotid stenosis, the authors stated:

"It is recommended that patients with asymptomatic carotid artery stenosis be screened for other treatable causes of stroke and that intensive therapy of all identified stroke risk factors be pursued (Class I, Level of Evidence C). The use of aspirin is recommended unless contraindicated because aspirin was used in all of the cited trials as an antiplatelet drug except in the surgical arm of 1 study, in which there was a higher rate of MI in those who were not given aspirin (Class I, Level of Evidence B). Prophylactic carotid endarterectomy is recommended in highly selected patients with high-grade asymptomatic carotid stenosis performed by surgeons with < 3% morbidity/mortality rates (Class I, Level of Evidence A). Patient selection should be guided by an assessment of comorbid conditions and life expectancy, as well as other individual factors, and be balanced by an understanding of the overall impact of the procedure if all-cause mortality is considered as one of the end points, and it should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences. Carotid angioplasty–stenting might be a reasonable alternative to endarterectomy in asymptomatic patients at high risk for the surgical procedure (Class IIb, Level of Evidence B); however, given the reported periprocedural and overall 1-year event rates, it remains uncertain whether this group of patients should have either procedure."

Liapis CD, Bell PRF, Mikhailidis D, Sivenius J, Nicolaides A, Fernandes J, Biasi G, Norgren L, on behalf of the ESVS Guidelines Collaborators. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. Eur J Vasc Endovasc Surg 2009;37:S1-S19.

Liapis and colleagues reported the European Society for Vascular Surgery evidence based guidelines on carotid stenosis interventions. They used the Agency for Healthcare Research and Quality (AHRQ) grading recommendations[7] and reported: "The European Society for Vascular Surgery brought together a group of experts in the field of carotid artery disease to produce updated guidelines for the invasive treatment of carotid disease. The recommendations were rated according to the level of evidence. Carotid endarterectomy (CEA) is recommended in symptomatic patients with > 50% stenosis if the perioperative stroke/death rate is < 6% [A], preferably within 2 weeks of the patient's last symptoms [A]. CEA is also recommended in asymptomatic men < 75 years old with 70-99% stenosis if the perioperative stroke/death risk is < 3% [A]. The benefit from CEA in asymptomatic women is significantly less than in men [A]. CEA should therefore be considered only in younger, fit women [A]. Carotid patch angioplasty is preferable to primary closure [A]. Aspirin at a dose of 75-325 mg daily and statins should be given before, during and following CEA. [A] Carotid artery stenting (CAS) should be performed only in high-risk for CEA patients, in high-volume centres with documented low peri-operative stroke and death rates or inside a randomized controlled trial [C]. CAS should be performed under dual antiplatelet treatment with aspirin and clopidogrel [A]. Carotid protection devices are probably of benefit [C]."

Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: A statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: Co-Sponsored by the Council on Cardiovascular Radiology and Intervention: The American Academy of Neurology affirms the value of this guideline. Stroke 2006:37;577-617.

This guideline provided "recommendations on the prevention of ischemic stroke among survivors of ischemic stroke or transient ischemic attack." Specific recommendations were as follows:

1.

"For patients with recent TIA or ischemic stroke within the last 6 months and ipsilateral severe 70% to 99%) carotid artery stenosis, CEA by a surgeon with a perioperative morbidity and mortality of < 6% (Class I, Level of Evidence A) is recommended. For patients with recent TIA or ischemic stroke and ipsilateral moderate (50% to 69%) carotid stenosis, CEA is recommended, depending on patient-specific factors such as age, gender, comorbidities, and severity of initial symptoms (Class I, Level of Evidence A). When the degree of stenosis is < 50%, there is no indication for CEA (Class III, Level of Evidence A) (Table 4)."

2.

"When CEA is indicated for patients with TIA or stroke, surgery within 2 weeks is suggested rather than delaying surgery (Class IIa, Level of Evidence B)."

3.

"Among patients with symptomatic severe stenosis (> 70%) in whom the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA, CAS is not inferior to endarterectomy and may be considered (Class IIb, Level of Evidence B). CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4% to 6%, similar to that observed in trials of CEA and CAS (Class IIa, Level of Evidence B)."

4.

"Among patients with symptomatic carotid occlusion, EC/IC bypass surgery is not routinely recommended (Class III, Level of Evidence A)."

6.Professional Society Position Statements

No new professional society position statements have been released since the last reconsideration of this policy.

7. Public Comments

During the initial 30-day comment period CMS received 79 comments. Comments in support of a coverage expansion were in the majority, but they present a diverse array of suggestions for coverage of various patient populations falling both within FDA approved indications and outside of those indications. These comments are summarized in the proposed decision memorandum.

During the 30-day comment period following the release of the proposed decision memorandum, we received a total of 41 comments from physicians, the public, four medical device companies, one insurance association and a coalition of medical specialty societies on one or more aspects of the proposed decision. The comments are summarized below. CMS responses to the comments are provided in italics. A complete list of references cited by commenters is available in the appendices.

Comments with New Evidence

During this comment period, no comments were submitted with new evidence on carotid artery stenting that has not been reviewed in either this analysis or previous analyses.

Comments Citing Prior Evidence

We have incorporated comments citing previously reviewed evidence into the comment section below. This section also includes comments about the interpretation of specific evidence, with CMS response. A complete list of citations referenced during this public comment period is available in Appendix C.

SAPPHIRE
Comment: One commenter contends that SAPPHIRE, "the only randomized trial for high surgical risk patients that will ever be done," demonstrates non-inferiority of CAS and when analyzed by treatment received actually demonstrates superiority of CAS to surgery.

Response: It is unfortunate that there is a belief that additional randomized trials will not be conducted. We have noted the limitations of the SAPPHIRE trial in past decisions and the need for supporting randomized trial evidence. The evidence is especially limited for asymptomatic patients as noted in the articles by Naylor (2009) and Abbott (2009). In addition, the SAPPHIRE trial was designed as a non-inferiority trial and thus conclusions about superiority of either intervention are not within the bounds of the trial design.

CAPTURE 2/EXACT Studies

Comments: One commenter asserts that the CAPTURE 2 and EXACT studies were conducted in a scientifically rigorous manner that involved pre-procedure patient interviews and post-procedure evaluations by independent neurologists as well as independent adjudication of all strokes and suspected strokes. This commenter further contends that the combined 30-day death or stroke rate for the two studies was 6.4% for all high risk symptomatic patients and 3.2% for all high risk asymptomatic patients and that these results are "in line with the AHA guidelines for intervention of 6% and 3%." For patients with anatomic risk factors, the combined 30-day stroke or death rates were 2.7% for asymptomatic patients and 1.7% for symptomatic patients, "within the AHA intervention guidelines." This commenter also asserts, "CMS gave more weight to studies with negative results and limited consideration to studies with positive results such as CAPTURE 2/EXACT and SAPPHIRE Worldwide." Furthermore, CMS did not consider flaws in negative studies and misinterpreted aspects of the CAPTURE 2 and EXACT studies.

Another commenter addresses CMS' concern regarding the different proportion of patients identified as at anatomic high risk in CAPTURE 2 and EXACT as compared to in SAPPHIRE Worldwide stating that in SAPPHIRE Worldwide patients with contralateral occlusions were included in the analysis, but were not included in the CAPTURE 2/EXACT analysis. CAPTURE 2 and EXACT also identified patients as at "anatomic high risk, exclusive of the presence of any comorbidity…in order to allow for a more precise estimate of 30-day outcomes." In response to CMS' criticism of the inclusion of an analysis of 30 day stroke or death rates for patients under age 80 in CAPTURE 2/EXACT, the commenter notes that this analysis was included because the AHA guidelines were established using a patient population of the same age. Another commenter suggests that data from EXACT, CAPTURE 2 and SAPPHIRE WW show "consistent results that should be recognized as valid and may provide better guidance than older trails which may not reflect contemporary outcomes."

Response: Although stroke or death rates of 6.4% and 3.2% may be "in line with" AHA guidelines, they do not meet the AHA guidelines of 6% and 3%, respectively. These short-term risks of death or stroke outweigh potential future benefits of stroke prevention. CMS has noted that the stroke or death rates approach the AHA guidelines, which is an accurate reflection of the rates reported in these studies. The CAPTURE 2 /EXACT results for anatomic risk factors were not supported by the overall results which did not meet the AHA guidelines. The anatomic risk subgroup represented only 7% of the study population. We noted this was far less than other studies and the consequent concerns and limitations in interpreting these subanalyses, particularly a potential for bias. The CMS analysis incorporates the totality of the evidence and does not weigh more recent studies more heavily than the original evidence.

Comments: Several commenters state that the results from EXACT, CAPTURE 2 and SAPPHIRE WW, in patients < 80 years old, demonstrate 30-day death or stroke rates of 5.3% for symptomatic patients and 2.9% for asymptomatic patients, which meet AHA guidelines. Several commenters note that this population is comparable to the population used to establish the AHA guidelines. One commenter asserts that available evidence also shows that patients age 80 and above can safely undergo CAS with comparable stroke or death rates to younger patients. Another commenter contends that CAS is a preferred option over CEA for high risk patients ≥ 80 years old based on three recently published peer-reviewed manuscripts.

Response: As noted in our analysis, 30 day death or stroke rates that selectively exclude about 23% of the study population to meet thresholds are difficult to interpret. We believe the exclusion of patients ≥ 80 years old may bias or confound the results of these studies. With respect to octogenarians, as the average age of Medicare beneficiaries increases, we must carefully consider coverage implications in this patient population. CMS cannot solely consider outcomes data that exclude octogenarians when making reasonable and necessary decisions. We also disagree with the contention that patients ≥ 80 years old have comparable outcomes to patients < 80 years old as noted in our analysis.

Sidawy and deDonato Studies

Comment: One commenter believes that CMS fails to recognize the flaws of the Sidawy study, which is a registry using self reported outcomes. The study does not have the clinical outcomes rigor of CAPTURE 2 and EXACT. In examining the de Donato et al study to compare CAS outcomes at 1 year with the ACAS outcomes within the same timeframe is not valid and there are inherent limitations to retrospective analyses. Because the study examines long term data, "the analysis is biased towards selecting patients with long term data only" and the data analyzed included early CAS procedures when embolic protection devices were not used.

Response: As noted in the evidence section, we incorporate all evidence from prior decisions and evaluate studies that were published since our last decision. These included the studies by Sidawy and de Donato. We noted the importance of long term outcomes, as reported by de Donato and Zarins, in this decision and prior decisions. As with most studies, there are limitations but these 2 studies were the only studies identified in our search that reported long term outcomes.

Evidence Requirements

Comments: One commenter contends that it is unrealistic for CMS to require data from randomized controlled trials in order to expand coverage and that single arm studies can be valid mechanisms to gather treatment and outcome data. This commenter asserts that "it is reasonable that CMS base carotid stenting coverage for the high -risk population on the extensive FDA IDE and the real-world trial data available and which was requested by CMS." Another commenter expresses concern with "the notion that CMS will require randomized controlled clinical trials to support further expansion of coverage." Another commenter argues that completing a randomized controlled trial comparing CAS to medical therapy is not realistic as physicians would likely consider such trial unethical and patients would resist randomization in favor of "a more immediate, clinically proven intervention."

Response: Randomized controlled trials are the gold standard for evidence and as such, data from RCTs is always preferred. We have noted the need for RCTs in prior decisions. The need for additional RCTs has been noted by respected carotid researchers as well (Ederle, 2009; Naylor, 2009; Abbott, 2009). We believe that coverage can be expanded based on non-RCT data. However, that data must be of adequate quality, relevant to the Medicare population and show outcomes that clearly provide a health benefit to Medicare beneficiaries. Based on our evidence review and analysis, we do not believe that currently available data meet these requirements. We do not believe it is unethical to conduct an RCT comparing CAS to optimal medical therapy, especially for asymptomatic patients, since there is no comparative evidence at this time. For stroke prevention, long term outcomes are important.

Other Comments

Coverage

Comments: Fourteen commenters support the proposed decision to not expand coverage. Three commenters contend that coverage should not be changed until the results of CREST are known. One commenter asserts that study results show CAS to be a poor second choice compared to CEA and another commenter argues that CEA has shown low morbidity and mortality in outstanding short term and long term data and CAS should be required to show the same results before coverage is expanded.

Response: We agree that currently available evidence does not support an expansion of coverage and have finalized the proposed decision.

Comments: Thirty one commenters disagree with the proposed decision to not expand coverage. Three commenters assert that CAS in high risk patients should be supported and reimbursed and two commenters contend that CMS coverage should match FDA approved indications. Two commenters argue that ample evidence exists to support CAS in patients that are too high risk for CEA. One commenter notes that at least two peer-reviewed publications demonstrate better CAS outcomes than the AHA standards; one commenter asserts that available data supports expanded coverage and one commenter contends that published data and proof of safety and efficacy have been provided to CMS so coverage should be expanded. One commenter asserts that data shows CAS in high risk symptomatic patients to be equally efficacious if not superior to CEA. One commenter contends that studies have shown 30-day stroke or death rates in CAS meet CEA guidelines. One commenter argues that studies have shown CAS to be valuable and another commenter asserts that studies have shown CAS to be safe and effective. Another commenter argues that CAS demonstrates better results when performed by well trained individuals and two commenters contend that CAS is safe and effective when performed by the right individuals on the right patients. One commenter supports coverage in patient groups where the risk to patients of no intervention is high and the odds of benefit are good.

Response: As noted above and in the evidence review, analysis and discussion sections of this document, CMS disagrees with these interpretations and has determined that currently available evidence is not sufficient to find that an expansion of coverage is warranted under §1862(a)(1)(A). In particular, the evidence does not demonstrate that CAS can be performed with assurance that the patients will benefit from the procedure in clinical practice. CMS has determined that coverage of the remaining FDA approved indications is not reasonable and necessary to treat when those procedures are performed outside of clinical trials or studies.

Comments: One commenter supports an expansion in coverage because CAS is less traumatic, and costly, and requires a shorter length of stay. Another commenter asserts that CAS is easier on patients, and results in reduced infection, bleeding and hospitalization and the procedure is less invasive. Another commenter supports expanded coverage of CAS because patients do not undergo general anesthesia and patients recover more quickly, require fewer days in the hospital and are not required to stop taking antiplatelet medications. One commenter contends that CAS is better than surgery because patients have no pain, no wound recovery and are home the next day, and the procedure is lower cost and lower risk.

Response: While CMS understands the potential benefits CAS may provide to certain patients in comparison to CEA, coverage determinations are based on clinical evidence and at this time, CMS has determined that currently available evidence does not support an expansion of coverage.

Comments: One commenter asserts that CAS is preferred in patients who have had laryngectomy and radiation induced carotid stenosis. Another commenter states that coverage is needed for patients with recurrent asymptomatic stenosis at the site of previous CEA. One commenter recommends expanding coverage when experienced physicians are performing CAS and require strict credentialing for those without experience in CAS. Another commenter notes "that the proposed decision memo does not include any specific analysis to support its conclusion that coverage should not be expanded to" symptomatic patients with 50-70% stenosis.

Response: As noted in the evidence section, we incorporate all evidence from prior decisions and evaluate studies that were published since our last decision. The CAPTURE 2/EXACT results for anatomic risk factors were not supported by the overall results which did not meet the AHA guidelines. The anatomic risk subgroup represented only 7% of the study population. We noted this was far less than other studies. We have also noted other concerns and limitations in interpreting these subanalyses. For symptomatic patients with 50-70% stenosis, the evidence is also insufficient and more limited by the smaller sample sizes (only about 10% of patients in CAPTURE 2/EXACT were symptomatic). In addition, there is disagreement about the need for carotid intervention for lesions with lower stenosis since the symptoms may not be due to the carotid findings but other causes. We focused on asymptomatic patients since these patients have made up the large majority of the studies and a more careful analysis is warranted to ensure that there is more benefit than harm.

Use of Embolic Protection Devices
Comments: Two commenters support the proposed inclusion of FDA cleared embolic protection devices in the NCD language in order to clearly communicate that FDA approved and cleared embolic protection devices are covered under the NCD.

Response: We agree that the addition of this language is important in order to clearly cover FDA approved and cleared embolic protection devices. We have revised language regarding embolic protection in section B3 that deals with coverage in FDA approved post approval studies, as well as in section B4 which deals with coverage outside of post approval studies and other clinical trial settings.

Comment: One commenter asserts that it is not in patients' best interest to have surgery or stenting for 70-80% asymptomatic stenosis.

Response: We agree that evidence does not support coverage of stenting outside of clinical trials and studies for patients with asymptomatic stenosis of 70-80%, however an examination of surgery in the same patient population is outside the scope of this NCD.

Need for Treatment Options
Comments: Two commenters assert that coverage should be expanded because patients and physicians should have a choice in treatment options for carotid stenosis. Two commenters contend that patients should have the option of CAS and one commenter contends that physicians need the option of CAS. One commenter argues that expanded coverage is needed because post approval extension studies are ending soon which will eliminate accessibility to CAS for asymptomatic patients. Another commenter contends that an expansion of coverage is appropriate in order to provide beneficiaries with anatomic risk factors, for whom "CEA is a relative or absolute contraindication," an option for treatment that does not require significant out of pocket expenses. One commenter states that "Americans deserve a less invasive, nonscarring option," and contends that CMS should encourage surgeons to learn to perform CAS and not be bullied by the surgical lobby. One commenter asserts that best medical management in patients with 80% stenosis with limited intracranial collateralization is "basically sending these patients home with stroke or death warrant."

Response: NCDs are based on evidence and not on a perceived need to offer medical options. CMS would like to point out that Medicare beneficiaries may be prescribed medical therapy, which is an alternative to CAS and CEA. Moreover, beneficiaries continue to have access to CAS in IDE, post approval studies and post approval extension studies, which are still ongoing. Some studies have yet to request continued coverage as post approval extension studies. This means that not only are post approval studies ongoing, but CMS fully expects future requests to continue covering asymptomatic patients in post approval extension studies. Once the results of ongoing studies are available, the evidence may support a change in Medicare coverage.

Stakeholder Agreement

Comments: Two commenters state that every specialty society that commented during the initial 30-day comment period of this reconsideration agreed to an expansion of coverage. One commenter also references a CAS stakeholders meeting held in 2007 during which multispecialty societies agreed that coverage should be expanded if CAS outcomes in high risk patients were able to conform to AHA guidelines and if consensus among societies could be achieved in support of expanded coverage. This commenter asserts that both of these goals have been achieved and thus coverage should be expanded.

Response: While numerous specialty societies expressed support for expanded coverage, some of these societies expressed support contingent upon a CMS requirement for facilities providing CAS to participate in a multispecialty society accreditation program with mandatory registry data submission and benchmark requirements. We summarized the views of these societies in the proposed decision memorandum. Currently no multispecialty society accreditation program is operational. Therefore, the conditional coverage supported by some of these societies would not yet be feasible.

Reviews by Insurance Companies

Comments: One commenter stated that the Blue Cross Blue Shield Association (BCBSA) technology assessment is also not relevant to this analysis because it was conducted in 2007 and did not include the most recent CAS data. Another commenter notes that CMS should consider that the BCBSA is currently reconsidering its negative assessment of CAS and reminds CMS that the BCBSA provides technology assessments and does not make coverage decisions. Most commercial BCBSA plans cover the FDA approved indications for CAS.

Response: NCDs are based on the currently available evidence rather than evidence reviews in progress or the coverage policies of private insurance companies.

CMS Evidence Review

Comments: One commenter cites the comments they submitted during the initial comment period and notes that no subsequent additional publications on clinical data have been generated. One commenter states that the "Analysis by CMS is fairly thorough, but lacks focus." Another commenter contends that CAS is being held to a higher standard than CEA. One commenter asserts that the decision not to cover CAS for asymptomatic stenosis > 80% appears to be financial and not in the best interest of the patient. One commenter contends that CMS is not taking advantage of knowledgeable consultants and is being influenced by an uninformed and vocal minority.

Response: During the evidence review process, CMS examines all available evidence carefully, including public comments, and does not consider external factors in making final coverage determinations. Cost was not a consideration in this decision. The decision was made based upon a thorough and accurate review of currently available evidence.

Additional Comments

Comments: One commenter asserts that expanded coverage would undermine enrollment in studies and trials examining the effectiveness of CAS. One commenter asserts that it is inappropriate for the government to dictate the practice of medicine. Another commenter states that "CMS should not include in their duties dedication to limiting innovation and the development of better, safer, and many times more appropriate means of treating any disease. No matter the political-economic climate." One commenter contends that the push for expanded coverage has been made by industry which stands to make a lot of money if coverage is expanded. One commenter requests that CMS "not let interest groups and rich compan[ies] looking to make a buck influence your decisions." One commenter states that the "recent draft decision… puts CMS in breach of its own public commitment to expand coverage" and that without expanded coverage Medicare beneficiaries remain at an unnecessary risk of surgery which does not improve the health benefit of beneficiaries "which is CMS' primary directive."

Response: As noted above, coverage determinations are based on evidence, and not on other external factors whether societal or industry-specific. Coverage decisions do not dictate the practice of medicine. In making a national decision on whether an item or service is reasonable and necessary to treat an illness or injury, we focus on medical and scientific evidence. At this time, additional research is still being conducted, which may add to the totality of evidence and ultimately justify a modification of current coverage policy.

Clinical Trial Coverage/Needs

Comments: One commenter states that well designed and conducted trials should be eligible for coverage. One commenter asserts that clinical trials must be prospective and randomized and not registries.

Response: Medicare covers CAS for patients enrolled in well designed and conducted trials as listed in the NCD (Appendix B):

- *Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);*
- *Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).*

CMS agrees that the most useful, highest quality evidence would result from RCTs, but also believes that valuable information may result from less rigorous studies and trials. However, the currently available evidence from less rigorous studies is not sufficient to expand coverage as outlined in the next section, Analysis.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act §1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a)(1)(A)of the Act. This section presents the agency's evaluation of the evidence considered and conclusions reached for the assessment.

The evidence base for carotid artery stenting continues to be of lower methodological quality. There are a small number of randomized trials comparing CAS and CEA, which have limited quality as we have discussed in prior decision memoranda. Acknowledging that existing case series and reviews may be markedly limited by selection bias, they are nonetheless informative in highlighting several other differences between treatments for carotid narrowing. We have focused on patients with asymptomatic stenosis ≥ 80% because of the expressed interest of the public, physicians and manufacturers. There is a considerable increase in CAS for patients with asymptomatic stenosis as reported in the published registry studies. As with any test or therapy for individuals with no symptoms, a careful, judicious consideration of risks and benefits needs to be conducted with patient input. CAS for patients with symptomatic stenosis ≥ 70% is covered and there appears to be less disagreement about carotid interventions for patients with symptomatic stenosis 50-70%.

a. **Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients at high risk for adverse events related to CEA with carotid artery stenosis ≥ 80% improves health outcomes compared to carotid endarterectomy or optimal medical therapy outside the IDE clinical trial or post approval study setting?**

Our initial decision to cover percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for high risk asymptomatic patients with carotid artery stenosis ≥ 80% in clinical studies[8] (http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=157) was based primarily on the SAPPHIRE trial (n =237 high risk patients with asymptomatic carotid artery stenosis ≥ 80%) results. At the time, we had many concerns about the quality of the SAPPHIRE trial and the lack of supporting evidence from other studies, which led to the existing coverage restricted to IDE trials and post approval (post marketing) studies required by the FDA. We also noted the need for additional randomized controlled trials comparing CAS to both CEA and optimal medical therapy and the need for long term follow-up especially in asymptomatic patients who have a low risk of stroke. Since then no additional randomized controlled trials that have enrolled asymptomatic patients have been completed and published. SPACE and EVA-3S enrolled only symptomatic patients. The CAVATAS-MED trial reported by Ederle and colleagues started enrollment (1992) before the availability of carotid stents (1994) and did not provide any new data or evidence since the number of patients who underwent CAS and symptoms status were not reported. Although this study was recently published, we also do not believe it is directly applicable since the original CAVATAS (2001) was designed primarily to study angioplasty alone and not CAS (as noted in our prior decision). Several trials (CREST, ACT, TACIT, SPACE2) are ongoing or in development that will directly compare CAS, CEA and possibly optimal medical therapy.

Since our last decision, one registry study by Sidawy and colleagues compared CAS to CEA and found a significantly higher rate of 30 day death, stroke or myocardial infarction in patients undergoing CAS compared to CEA (5.72% vs. 2.63%; P value < 0.001) for all patients in the registry. A follow-up analysis of the CaRESS study was also published which reported no difference in death/stroke rates between CEA and CAS at 4 years for the combined group of high risk patients. It is very important to see long term outcomes; however, the results did not support CAS for stroke prevention in asymptomatic patients (4 year death/stroke rate of 25.8%). Also, as we noted in prior decisions, the CaRESS study did not focus on high surgical risk patients and enrolled a small number of these patients that underwent CAS (n=77).

Several CAS only registry studies (Gray, Massop, Sidawy, de Donato) have been published. The study by de Donato and colleagues reported 5 year outcomes for 3179 patients who underwent CAS. Of these, 1317 had symptomatic lesions ≥ 50% while 1862 had asymptomatic lesions ≥ 80%. For asymptomatic patients, death or stroke was 3.5% at year 1 increasing to 26.1% at year 5, similar to the CaRESS results. The annual stroke rate was 1.9% which is higher than reported rates from prior CEA trials. This is concerning since the patients in this study were generally not high risk patients. The outcomes for asymptomatic patients were not significantly different (overlapping 95% confidence intervals) from the outcomes for symptomatic patients (2.5% and 3% at year 1 increasing to 16.7% and 18.7% at year 5, respectively), which is also concerning since symptomatic patients are known to be at higher risk for morbidity and mortality in general. One would expect based on prior evidence that asymptomatic patients would have better outcomes than symptomatic patients. Given that these 2 studies were registry studies, the evidence is less definitive but nonetheless concerning and further stress the need for additional long term data from randomized controlled trials. The registry studies by Gray (2009), Massop (2009) and Sidawy (2009) reported 30 day outcomes only. For stroke prevention, especially for asymptomatic individuals, longer term data are required to determine if the intervention actually prevents strokes. Since our decision to cover CAS in clinical studies, several thousands of patients have undergone the procedure in registry studies with no comparison groups. Yet randomized controlled trials comparing CAS to CEA and CAS to optimal medical therapy, especially in asymptomatic patients, have not been completed and reported. In light of Abbott's review, the need for randomized controlled trials of CAS compared to optimal medical therapy is further highlighted.Naylor and colleagues also emphasized the ongoing need for randomized controlled trials: "At a time when evidence suggests that up to 94% of interventions may not benefit the patient, the authors urge that at least one of the randomised trials comparing CEA with CAS in asymptomatic patients includes an adequately powered third limb for BMT [best medical therapy]. Timely investment now could optimise patient care and resource utilisation for all of us in the future."

Since there are no new completed, published randomized trials and 2 nonsupportive registry studies, there is insufficient evidence to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients with carotid artery stenosis ≥ 80% improves health outcomes compared to carotid endarterectomy or optimal medical therapy outside the clinical trial or post approval study setting.

This conclusion is consistent with the Cochrane reviews by Ederle (2007, 2009) and the evidence based guidelines from the European Society for Vascular Surgery that noted: "Carotid artery stenting (CAS) should be performed only in high-risk for CEA patients, in high-volume centres with documented low peri-operative stroke and death rates or inside a randomized controlled trial." This is also consistent with the Blue Cross Blue Shield Association Technology Assessment Center (TEC) which has maintained that CAS with distal embolic protection does not meet TEC criteria since 2007 ("Available evidence does not support concluding that CAS with EPD improves the net health outcome among patients at average or increased medical risk." Full report at: http://www.bcbs.com/blueresources/tec/vols/22/22_01.pdf).

b. **Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors for CEA associated adverse events with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% improves health outcomes?**

While we have not completely defined what constitutes high risk for CEA and have given discretion to classifications used in the published studies, we have been aware of the potential variability among patients considered to be at high risk. In the SAPPHIRE trial (Yadav, 2004), several criteria were used to classify high risk patient selection. These included: "Clinically significant cardiac disease (congestive heart failure, abnormal stress test, or need for open-heart surgery), Severe pulmonary disease, Contralateral carotid occlusion, Contralateral laryngeal-nerve palsy, Previous radical neck surgery or radiation therapy to the neck, Recurrent stenosis after endarterectomy, Age > 80 yr." The most common anatomic high risk factor was contralateral carotid occlusion (24%), followed by CEA restenosis (23%). Since then, there appears to be some coalescing of thought of researchers, professional societies and device manufacturers that the subset of anatomic high risk factors, such as contralateral carotid occlusion, prior radical neck surgery or radiation therapy to the neck, restenosis after CEA, high internal carotid lesions that are difficult to access surgically, presents more challenges to CEA than the subset with comorbid diseases, such as severe cardiac or pulmonary disease.

Although no randomized controlled trials have been reported that compare CAS to CEA or optimal medical therapy as noted above, several post approval studies and inhospital analyses have been published since our last reconsideration (October, 2008) that evaluated patients undergoing CAS and anatomic high risk factors. Three studies evaluated 30 day outcomes (Gray, 2009; Massop, 2009; Sidawy, 2009). The studies by Zarins (2009), de Donato (2009), Kawabata (2009), Simonetti (2009), Steppahcer (2009) and Vogel (2009) did not report outcomes for anatomic high risk factors.

In the EXACT/CAPTURE 2 study, Gray and colleagues reported: "The 30-day rate of death and stroke for the 60 symptomatic patients with anatomic factors was 1.7% (95% CI, 0.0% to 8.9%); the single stroke was adjudicated as major. The 30-day rate of death and stroke for the 371 asymptomatic patients with anatomic high -risk features was 2.7% (95% CI, 1.3% to 4.9%), of which 78% were minor." In the SAPPHIRE WW study, Massop and colleagues reported: "Asymptomatic patients with anatomic risk factors had a 30-day stroke and death rate of 1.8% while symptomatic patients with anatomic risk factors had a 30-day rate of 4.5% (P = 0.0589)." The death or stroke rate for patients with pure anatomic risk factors was 2.5% (18/716). The studies by Sidawy (2009), Steppacher (2009) and Vogel (2009) did not report specific results for anatomic high risk factors.

Of the two studies that reported results for patients with anatomic high risk factors, combined 30 day death and stroke was 2.6% in the Gray study and 2.5% in the Massop study. The proportion of patients classified as anatomic high risk was about 7% (431/6320) in the Gray study and 37% (716/1961) in the Massop study. This large discrepancy needs further consideration. In the SAPPHIRE trial (2004), the combined proportion of patients with the two most common high risk criteria, contralateral carotid occlusion or recurrent stenosis after endarterectomy, was up to 46% (if the separate rates of 24% and 22% did not overlap). The proportion of patients with anatomic high risk criteria in the SAPPHIRE WW registry was consistent with the SAPPHIRE trial; however, the markedly lower proportion (7%) in the EXACT/CAPTURE 2 registry suggests either classification / reporting errors or selection bias (selective enrollment of lower risk patients).

The study by Gray and colleagues reported that CAS outcomes have met the AHA/ASA recommendations for high surgical risk patients < 80 years of age. Since outcomes for patients $\geq$ 80 years old were worse, the selective exclusion of this subgroup of patients also raises questions. Exclusion of 23-24% of the patients presents great potential for selection bias or extreme confounding in the results. CAS continues to be performed in large numbers for patients $\geq$ 80 years, so results excluding these patients do not accurately reflect current practice realities. The study by Gray presents interesting findings from registry data that generate hypotheses but further evidence from clinical trials is needed to confirm these findings. The study by Massop did not report results by symptoms or by age other than noting age $\geq$ 80 years was a significant predictor of 30 day major adverse events.

For symptomatic and asymptomatic patients with anatomic high risk factors, the 30 day adverse event rates appear to approach the AHA/ASA recommendations; however, the inherent flaws of registry studies, such as lack of control groups, patient selection bias and voluntary data submission, limit the interpretation of the published death and stroke rates and reduce the strength of this evidence considerably. Results of subgroup analyses of registry studies are even more problematic to interpret and are at best only suggestive.

In summary, while available evidence suggests the potential for PTA of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% to improve health outcomes, currently published data are not sufficient to expand coverage beyond the currently covered patient populations. The current evidence, which has been collected under the authority of coverage for post-approval studies, is insufficient to conclude that PTA of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% can be performed with procedural complication rates to meet AHA/ASA guidelines. Due to the lower quality and limited quantity of published, peer-reviewed evidence available addressing the patient populations under consideration, CMS has determined that an expansion of coverage is not reasonable and necessary and has decided to make no changes to the NCD.

Carotid Interventions in Patients ≥ 80 years of Age

Most of the large trials that demonstrated the benefits of CEA excluded patients ≥ 80 years of age. The SAPPHIRE trial (Yadav, 2004) showed that patients ≥ 80 years of age had significantly higher 30 day adverse events. A number of registry studies (SAPPHIRE WW, EXACT/CAPTURE 2, SVS Vascular Registry) and 1 meta-analysis (Usman, 2009) have also shown that patients ≥ 80 years of age have higher rates of 30 day adverse events. The 2006 AHA/ASA guidelines noted: "Despite the need to consider different interventional approaches, some trials do not include a sufficient number of subjects > 80 years of age to fully evaluate the efficacy of a therapy within this important subgroup." While cautions have often been raised, the numbers of patients ≥ 80 years undergoing CAS have increased. In the SAPPHIRE trial, the proportion of CAS patients > 80 years was 19% (32/166). This proportion increased to 26% (520/2001) in SAPPHIRE WW, 24% (511/2145) in EXACT, 24% (829/3,500) in CAPTURE and 22% (938/4175) in CAPTURE 2. As with many procedures in the elderly, the key question is should it be done and not whether it can be done. To answer this for patients ≥ 80 years of age, a consideration of long term health outcomes and life expectancy is needed in addition to the peri-procedural health outcomes reported in various case series and registry studies.

Since the natural history of disease on optimal medical therapy is unknown for these patients, long term outcomes are extremely important to determine whether CAS should be performed. No published study has presented long term outcomes for patients ≥ 80 years. For carotid interventions, a life expectancy of at least 5 years is recommended by the AHA/ASA. However, if the life expectancy is less than 5 years, the potential benefits of carotid interventions may not be realized (to overcome the peri-procedural adverse events). For asymptomatic patients, CAS enters the realm of primary prevention of stroke and a more rigorous evaluation of health risks and benefits with definite evidence is desperately needed.

Until long term results from randomized controlled trials comparing CAS to optimal medical therapy are available for this important subgroup, CAS and possibly any carotid intervention should rarely, if at all, be performed in patients ≥ 80 years of age especially for asymptomatic individuals.

Embolic Protection Devices

As carotid stenting continues to be widely performed, new embolic protection devices, without specific accompanying stent systems, have been developed and several have received FDA 510(k) clearance as substantially equivalent to previous embolic protection devices. In order to avoid confusion and clearly include these newer devices, we are revising the NCD language addressing EPDs, the use of which is required for Medicare coverage of PTA of the carotid arteries concurrent with stenting, to specifically include coverage of "FDA approved or cleared embolic protection devices." As EPDs that are designed to be placed proximally are being developed and cleared by the FDA, we have determined to remove "distal" from references to embolic protection devices to avoid confusion. With the advent of proximal embolic protection as a counterpart to distal devices, we believe that the use of embolic protection is always possible. Omission of embolic protection raises patient safety issues, therefore we are also revising coverage language to clearly state that a CAS procedure performed without embolic protection is not covered by Medicare.

Summary

As we have concluded in the last two decision memoranda, "for CAS to be considered an alternative to CEA and improve health outcomes for asymptomatic patients with asymptomatic stenosis > 80%, the perioperative morbidity and mortality rates should be less than 3%." For symptomatic patients with stenosis > 50%, the benchmark is less than 6% death and stroke within 30 days of the procedure. The body of randomized trials and post approval studies does not demonstrate that CAS can be performed at that level. Although performance continues to improve, the greatest concern is for asymptomatic patients who are at low risk and may benefit from medical therapy. Some experts have questioned the 3% value, as the benefits of medical therapy may have improved. This continues to highlight the need for a randomized trial comparing CAS with optimal medical therapy. Since current evidence is inadequate, CMS has decided not to expand coverage of PTA concurrent with carotid artery stenting.

IX. Conclusion

The Centers for Medicare and Medicaid Services (CMS) has determined, based on the Food and Drug Administration (FDA) clearance of new embolic protection devices, to revise the national coverage determination (NCD) language regarding embolic protection devices as follows in section B3 and B4 of the NCD:

Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent and an FDA-approved or cleared embolic protection device for an FDA-approved indication when furnished in accordance with FDA-approved protocols governing post-approval studies. CMS determines that coverage of PTA of the carotid artery is reasonable and necessary in these circumstances.

Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent for the following:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis $\geq$70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or cleared embolic protection devices. *If deployment of the embolic protection device is not technically possible, and not performed, then the procedure is not covered by Medicare;*
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis $\geq$80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).

We have decided to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare NCD Manual 20.7B). We have decided to retain our existing coverage policy with a slight revision to the language regarding embolic protection devices.

Appendix A: General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine whether: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

CMS normally divides the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)

- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens, and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease, and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing, and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow -up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation), and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations because one of the goals of our determination process is to assess health outcomes. We are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Improved health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary.For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix B: Changes to the National Coverage Determination

Effective XX, 2009, Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent with embolic protection for the following:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis ≥70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or cleared embolic protection devices. *If deployment of the embolic protection device is not technically possible, and not performed, then the procedure is not covered by Medicare;*
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).

Coverage is limited to procedures performed using FDA approved carotid artery stents and FDA approved or cleared embolic protection devices.

The use of an FDA approved or cleared embolic protection device is required. If deployment of the embolic protection device is not technically possible, and not performed, then the procedure is not covered by Medicare.

Patients at high risk for CEA are defined as having significant comorbidities and/or anatomic risk factors (i.e., recurrent stenosis and/or previous radical neck dissection), and would be poor candidates for CEA.

Significant comorbid conditions include but are not limited to:

- congestive heart failure (CHF) class III/IV;
- left ventricular ejection fraction (LVEF) < 30%;
- unstable angina;
- contralateral carotid occlusion;
- recent myocardial infarction (MI);
- previous CEA with recurrent stenosis;
- prior radiation treatment to the neck; and
- other conditions that were used to determine patients at high risk for CEA in the prior carotid artery stenting trials and studies, such as ARCHER, CABERNET, SAPPHIRE, BEACH, and MAVERIC II.

Symptoms of carotid artery stenosis include carotid transient ischemic attack (distinct focal neurological dysfunction persisting less than 24 hours), focal cerebral ischemia producing a nondisabling stroke (modified Rankin scale < 3 with symptoms for 24 hours or more), and transient monocular blindness (amaurosis fugax). Patients who have had a disabling stroke (modified Rankin scale $\geq$ 3) shall be excluded from coverage.

The determination that a patient is at high risk for CEA and the patient's symptoms of carotid artery stenosis shall be available in the patient medical records prior to performing any procedure.

The degree of carotid artery stenosis shall be measured by duplex Doppler ultrasound or carotid artery angiography and recorded in the patient's medical records. If the stenosis is measured by ultrasound prior to the procedure, then the degree of stenosis must be confirmed by angiography at the start of the procedure. If the stenosis is determined to be less than 70% by angiography, then CAS should not proceed.

In addition, CMS has determined that CAS with embolic protection is reasonable and necessary only if performed in facilities that have been determined to be competent in performing the evaluation, procedure and follow-up necessary to ensure optimal patient outcomes. Standards to determine competency include specific physician training standards, facility support requirements and data collection to evaluate outcomes during a required reevaluation.

CMS has created a list of minimum standards modeled in part on professional society statements on competency. All facilities must at least meet CMS's standards in order to receive coverage for carotid artery stenting for high risk patients.

- Facilities must have necessary imaging equipment, device inventory, staffing, and infrastructure to support a dedicated carotid stent program. Specifically, high-quality X-ray imaging equipment is a critical component of any carotid interventional suite, such as high resolution digital imaging systems with the capability of subtraction, magnification, road mapping, and orthogonal angulation.

- Advanced physiologic monitoring must be available in the interventional suite. This includes real time and archived physiologic, hemodynamic, and cardiac rhythm monitoring equipment, as well as support staff who are capable of interpreting the findings and responding appropriately.

- Emergency management equipment and systems must be readily available in the interventional suite such as resuscitation equipment, a defibrillator, vasoactive and antiarrhythmic drugs, endotracheal intubation capability, and anesthesia support.

- Each institution shall have a clearly delineated program for granting carotid stent privileges and for monitoring the quality of the individual interventionalists and the program as a whole. The oversight committee for this program shall be empowered to identify the minimum case volume for an operator to maintain privileges, as well as the (risk-adjusted) threshold for complications that the institution will allow before suspending privileges or instituting measures for remediation. Committees are encouraged to apply published standards from national specialty societies recognized by the American Board of Medical Specialties to determine appropriate physician qualifications. Examples of standards and clinical competence guidelines include those published in the December 2004 edition of the American Journal of Neuroradiology, and those published in the August 18, 2004 Journal of the American College of Cardiology.

- To continue to receive Medicare payment for CAS under this decision, the facility or a contractor to the facility must collect data on all carotid artery stenting procedures done at that particular facility. This data must be analyzed routinely to ensure patient safety. This data must be made available to CMS upon request. The interval for data analysis will be determined by the facility but shall not be less frequent than every 6 months.

Since there currently is no recognized entity that evaluates CAS facilities, CMS has established a mechanism for evaluating facilities. Facilities must provide written documentation to CMS that the facility meets one of the following:

1. The facility was an FDA approved site that enrolled patients in prior CAS IDE trials, such as SAPPHIRE, and ARCHER;

2. The facility is an FDA approved site that is participating and enrolling patients in ongoing CAS IDE trials, such as CREST;

3. The facility is an FDA approved site for one or more FDA post approval studies; or
4.

   The facility has provided a written affidavit to CMS attesting that the facility has met the minimum facility standards. This should be sent to:

   Director, Coverage and Analysis Group
   7500 Security Boulevard, Mailstop C1-09-06
   Baltimore, MD 21244.

The letter must include the following information:
Facility's name and complete address;
Facility's Medicare provider number;
Point-of-contact for questions with telephone number;
Discussion of how each standard has been met by the hospital;
Mechanism of data collection of CAS procedures; **and**
Signature of a senior facility administrative official.

A list of certified facilities will be made available and viewable at: http://www.cms.hhs.gov/coverage/carotidstentfacilities.asp. In addition, CMS will publish a list of approved facilities in the Federal Register.

Facilities must recertify every two (2) years in order to maintain Medicare coverage of CAS procedures. Recertification will occur when the facility documents that and describes how it continues to meet the CMS standards.

The process for recertification is as follows:

At 23 months after initial certification:

- Submission of a letter to CMS stating how the facility continues to meet the minimum facility standards as listed above.

At 27 months after initial certification:

- Submission of required data elements for all CAS procedures performed on patients during the previous two (2) years of certification.
- Data elements: Patients' Medicare identification number if a Medicare beneficiary;
  Patients' date of birth;
  Date of procedure;
  Does the patient meet high surgical risk criteria (defined below)?
  - Age >80;
  - Recent (< 30 days) Myocardial Infarction (MI);
  - Left Ventricle Ejection Fraction (LVEF) < 30%;
  - Contralateral carotid occlusion;
  - New York Heart Association (NYHA) Class III or IV congestive heart failure;
  - Unstable angina: Canadian Cardiovascular Society (CCS) Class III/IV;
  - Renal failure: end stage renal disease on dialysis;
  - Common Carotid Artery (CCA) lesion(s) below clavicle;
  - Severe chronic lung disease;
  - Previous neck radiation;
  - High cervical Internal Carotid Artery (ICA) lesion(s);
  - Restenosis of prior carotid endarterectomy (CEA);
  - Tracheostomy;
  - Contralateral laryngeal nerve palsy.

  Is the patient symptomatic (defined below)?
  - Carotid Transient Ischemic Attack (TIA): distinct focal neurologic dysfunction persisting less than 24 hours;
  - Non-disabling stroke: Modified Rankin Scale < 3 with symptoms for 24 hours or more;
  - Transient monocular blindness: amaurosis fugax.

  Modified Rankin Scale score if the patient experienced a stroke;
  % stenosis of stented lesion(s) by angiography;
  Was embolic protection used?
  Were there any complications during hospitalization (defined below)?
  - All stroke: an ischemic neurologic deficit that persisted more than 24 hours;
  - MI;
  - All death.

Recertification is effective for two (2) additional years during which facilities will be required to submit the requested data every April 1 and October 1.

CMS will consider the approval of national carotid artery stenting registries that provide CMS with a comprehensive overview of the registry and its capabilities, and the manner in which the registry meets CMS data collection and evaluation requirements. Specific standards for CMS approval are listed below. Facilities enrolled in a CMS approved national carotid artery stenting registry will automatically meet the data collection standards required for initial and continued facility certification. Hospitals' contracts with an approved registry may include authority for the registry to submit required data to CMS for the hospital. A list of approved registries will be available on the CMS coverage website.

National Registries

As noted above, CMS will approve national registries developed by professional societies and other organizations and allow these entities to collect and submit data to CMS on behalf of participating facilities to meet facility certification and recertification requirements. To be eligible to perform these functions and become a CMS approved registry, the national registry, at a minimum, must be able to:

1. Enroll facilities in every US state and territory;

2. Assure data confidentiality and compliance with HIPAA;

3. Collect the required CMS data elements as listed in the above section;

4. Assure data quality and data completeness;

5. Address deficiencies in the facility data collection, quality and submission;

6. Validate the data submitted by facilities as needed;

7. Track long term outcomes such as stroke and death;

8. Conduct data analyses and produce facility specific data reports and summaries;

9. Submit data to CMS on behalf of the individual facilities;

10. Provide quarterly reports to CMS on facilities that do not meet or no longer meet the CMS facility certification and recertification requirements pertaining to data collection and analysis.

Registries wishing to receive this designation from CMS must submit evidence that they meet or exceed our standards. Though the registry requirements pertain to CAS, CMS strongly encourages all national registries to establish a similar mechanism to collect comparable data on CEA. Having both CAS and CEA data will help answer questions about carotid revascularization, in general, in the Medicare population.

CAS for patients who are not at high risk for CEA remains covered only in FDA-approved Category B IDE clinical trials under 42 CFR 405.201.

CMS has determined that PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent is not reasonable and necessary for all other patients.

Appendix C: References Cited by Commenters

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1 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/PMNSimpleSearch.cfm?db=PMN&id=K083300

2 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/PMNSimpleSearch.cfm?db=PMN&id=K082348

3 XACT post approval study information at: http://www.clinicaltrials.gov/ct2/show/NCT00287508

4 ACCULINK post approval study information at: http://www.clinicaltrials.gov/ct2/show/NCT00180492

5 The SAPPHIRE trial was "was a multicenter, prospective trial conducted at 29 centers between 2000 and 2002 to compare outcomes of CAS versus CEA in high-surgical risk patients. Entry criteria included either >50% carotid stenosis if symptomatic or >80% carotid stenosis if asymptomatic." (Yadav, 2004; Gurm, 2008) SAPPHIRE information at: http://www.clinicaltrials.gov/ct2/show/NCT00231270?term=sapphire&rank=12

6 SAPPHIRE WW information at: http://www.clinicaltrials.gov/ct2/show/NCT00403078?term=sapphire&rank=4

7 Grade Recommendation

A - Based on the criterion of at least one randomized, controlled clinical trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B - Based on well-conducted clinical studies but no good-quality randomized clinical trials on the topic of recommendation.

C - Based on evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. (i.e., no applicable studies of good quality)

8 Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis >80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the National Coverage Determination on CAS post approval studies (Medicare NCD Manual 20.7).

Back to Top

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Back to Top